RESPONSES TO COMMENTS SUBMITTED BY THE ALLIANCE OF AUTOMOBILE MANUFACTURERS (AAM).

I. General Comments

Comment 1: We applaud and support the efforts of the California legislature to protect infants and children against potentially adverse actions of toxic air pollutants. The success of environmental regulations in eradicating acute lead encephalopathy in infants, toddlers and children is widely accepted. In contrast to the effects of acute lead poisoning, however, the question of whether there are chronic effects of many air pollutants remains wide open in the scientific literature, even for regulated air pollutants such as ozone. Even though there is concern over adverse effects from chronic exposures to ambient toxic air contaminants, these effects remain undocumented (except for lead). We feel strongly that these questions should be resolved before the provisions of Senate Bill 25 are used for regulatory purposes. The OEHHA evaluation provides an opportunity to discuss these questions from all points of view and document the large gaps in scientific knowledge in this field.

Response 1: OEHHA thanks the Alliance for their support of the general objectives of the Children's Environmental Health Protection Act. OEHHA disagrees that questions of chronic effects of air pollution are "wide open" in the scientific literature. There are now a number of studies, described in detail in the joint ARB/OEHHA report "Adequacy of California Ambient Air Quality Standards: Children's Environmental Health Protection Act" available at www.arb.ca.gov, which document effects on pulmonary function in children from long-term exposure to air pollutants. In addition, many of the toxic air contaminants have a strong chronic toxicity and epidemiology database, which has been utilized to identify them as a toxic air contaminant. OEHHA is complying with the mandates provisions of SB25. While there are large gaps in scientific knowledge, we believe that we have identified sufficient evidence to prepare a list of five TACs, which may disproportionately affect infants and children.

II. Basis for concerns that infants and children are more susceptible than adults

Comment 2: The OEHHA draft was prepared on the basis of legislative concerns (SB 25, Section 1) that infants and children are more susceptible to the adverse effects of air pollution because:

(a) a greater dose of air pollutants is delivered to their lungs because of higher ventilation rates relative to their body weight and lung surface area

(b) potentially significant obstruction of children's airways can result from irritation or inflammation caused by air pollution because children have narrower airways than adults;

(c) children spend more time outdoors than adults;

(d) asthma attacks in infants and children are exacerbated by air pollution;

(e) developing organs and tissues are more susceptible to damage by "some" environmental contaminants .

In light of new scientific knowledge, there are several questions concerning these "findings." The OEHHA draft should address these factors and the questions we raise and verify whether or not the factors play a role in potentiating the effects of air pollution in children. SB 25 requires OEHHA to evaluate potential TACs "using current principles, practices and methods used by public health professionals who are experienced practitioners in the field of epidemiology, human health effects assessments, risk assessment and toxicity" (SB 25, 5b) and "assess the availability and quality of data on health effects including potency, mode of action and other relevant biological factors," assessing exposure patterns, susceptibility of infants and children to air pollutants, (specific) effects of toxic air contaminants, and interaction of multiple air pollutants (SB 25, 5c).

Unfortunately, the OEHHA draft is not fully responsive to these requirements and fails to recognize gaps in scientific knowledge concerning the susceptibility of children to the chronic action of toxic air pollutants. The limitations and uncertainties due to these gaps should be discussed extensively in the document. Because of the lack of knowledge, the draft often falls back on "default options," i.e., options used in the absence of convincing

scientific knowledge. Because risk assessment methodologies as well as the underlying science continue to evolve, the OEHHA document should allow departure from the default options "whenever new developments in science ascertain that there is a consensus among knowledgeable scientists that new scientific evidence justifies departing from the default options" (NAS/NRC 1994[1]).

Response 2: The comment refers to language in the identification of TACs rather than in the specific sections of the statute requiring OEHHA to develop the list of existing TACs that may cause infants and children to be especially susceptible to illness. The statute does not mandate OEHHA to identify all the gaps in the current scientific knowledge. The draft report follows language in Section 39669.5(a) which requires OEHHA to establish, in consultation with the ARB, a list of up to 5 toxic air contaminants (already identified as such) that may cause infants and children to be especially susceptible to illness. The language states that "in developing the list, the office shall take into account public exposures to toxic air contaminants, whether by themselves or interacting with other toxic air contaminants or criteria air pollutants, and the factors listed in subdivision (c) of Section 39660". These factors are:

(A) Exposure patterns among infants and children that are likely to result in disproportionately high exposure to ambient air pollutants in comparison with the general population.

(B) Special susceptibility of infants and children to ambient air pollutants in comparison to the general public.

(C) The effects on infants and children of exposure to toxic air contaminants and other substances that have a common mechanism of toxicity.

(D) The interaction of multiple air pollutants on infants and children, including the interaction between criteria air pollutants and toxic air contaminants.

[1] NAS/NRC Committee on Risk Assessment of Hazardous Air Pollutants, "Science and Judgment in Risk Assessment, National Academy Press, Washington, D.C., 1994;

In addition, the law describes requirements for both the evaluation of information on existing TACs and the evaluation of data for candidate TACs. The comment has focused on the language referring to candidate TACs and not on the portion of the statute for developing this list (subdivision c).

OEHHA is very conscious of the uncertainties in the evidence available for differential impacts of TACs on infants and children, and has attempted in the draft document to delineate both those data and conclusions in which some confidence may be placed, and those that are more provisional in nature. Some specific instances where the draft report may have been insufficiently clear as to the reliability of specific data or conclusions have been noted in the responses to other comments and will be corrected in the final document. The comment also seems to suggest that this evaluation is incomplete. However, this report is not a risk assessment; it is a hazard identification step. However, as in all risk assessment related activities, OEHHA is inevitably faced with drawing conclusions and making recommendations in the face of significant uncertainties. In responding to this situation OEHHA intends to follow the recommendations of both the original and subsequent NAS/NRC reports, and of various California risk assessment guidance documents, in using actual data where these are available, and standard assumptions in cases of uncertainty, coupled with standard scientific inference methods.

Comment 3: Specifically, the document should discuss claims that: <u>higher ventilation rates relative to body weight and lung surface area in infants and children result in a higher dose of the pollutant delivered to their lungs</u> and that these exposure patterns are "likely to result in disproportionately high exposure to ambient air pollutants in comparison with general population."(OEHHA 2000) While the document appropriately recognizes that no substantial differences exist between children and adults in the alveolar surface area in relation to body weight (Hislop, 1986), it fails to inform the reader that no scientific evidence supports a general statement that higher breathing rates in children can result in chronic accumulation of higher doses of all inhaled toxicants irrespective of their mechanisms of action.. Established pharmacokinetic principles document that the alveolar uptake and transition of inhaled non irritant, system-poisoning gases across the alveolar membrane depends primarily on their penetration rates across

the alveolar membrane and the rapidity of the transfer to their tissue depots by pulmonary circulation. In the absence of other gas action modes, these processes are solely governed by the concentration gradient between the alveolar air and blood and between the blood and tissue, respectively. If the alveolar penetration or gas removal by circulation are slow, no concentration gradients exists across the alveolar membrane and inhaled gases are exhaled without any additional transport into the organism. Breathing frequency alone, while capable of accelerating the achievement of a steady state between the alveolar air and circulating blood, does not, therefore, predetermine a higher cumulative dose of the gas in the body. Only when the rates of alveolar transport and transfer to tissue depots are fast or irritant gases react with the airway surface receptors, will increased ventilation contribute to a greater dose of the inhaled gas to the tissues or potentiate the irritative effects in the lung. Generalization of these processes for all toxic air pollutants seems to be, therefore, not appropriate unless the mechanism of the toxicant's action is known.

Response 3: The purpose of the OEHHA draft report is not to criticize the language of the statute. OEHHA discussed the issues of both breathing rate and ratio of alveolar surface area in the introductory sections of the draft report. In addition, the comment seems to imply that we are assuming that all substances act by a similar mode of action. Of course, this is not the case and is the reason why we have substance-specific summaries in the report. As noted in the comment, the pharmacokinetics of absorption across the lung vary by the physicochemical properties of the compound (such as solubility in plasma) as well as by physiological differences between infants, children, and adults. The introductory sections IIIA through D are not meant to be treatises but rather introductions to the concepts of why there may be differences in dose and effect between infants, children, and adults.

Comment 4: The document should discuss claims that: narrower airways in infants and children with asthma contribute to an obstruction of airways more than in adult asthmatics. These statements seem to be influenced by oversimplified mechanistic considerations rather than a proper understanding of the irritative response to inhaled air

toxicants (Lipsett, 1995). New morphometric data confirm the concept that the inner bronchial diameters are smaller in infants than in adults, but the assumption of easier bronchial obstruction fails to recognize that the epithelial cells of the airways are also smaller than in adults (Gehr, 1994[2]). The relative contribution of the epithelial height to inner bronchial diameter ratio represents, therefore, a relatively small change in proportion to the bronchial diameter (from 0.75 % in an adult vs. 1.93% in the 1yr.-old infant). These differences may not be of a magnitude that would substantially increase the possibility of bronchial obstruction due to irritated cells even in the asthmatic child. The significance and the role of the actual differences in magnitude should be discussed in the document before this assumption is accepted.

Response4: As noted in the responses above, the purpose of the draft OEHHA report is not to criticize the language of the statute. In response to the comment, however, it is a rather simple concept that it takes less bronchial secretion to block a smaller lumen than a larger lumen. In addition, the narrower the aperture through which air must flow, the higher the resistance, the harder it is to breathe.

Comment 5: The document should discuss claims that: children spend more time outdoors in comparison with adults. The fact that children's activity patterns differ from adults is not, in itself, a reason for more protective standards. Potentially higher outdoor exposures of children have been often cited in support of more protective standards. However, with the development of air-conditioned shopping malls and houses, the differences may not be large, particularly in areas with hot weather such as California. New observation studies suggest that the original estimates of differences between children and adults (Wiley et al., 1991) have changed with increasing levels of indoor climatization and are not as high at the present time as they were in the late 1980's. In addition, there are other differences in activity patterns between children and adults that need to be considered. Children also spend more time indoors at home and less time in

[2] Gehr, P., "Anatomy and Morphology of the Respiratory Tract", in Human Respiratory Tract Model for Radiological Protection, Annals of the ICRP, Publ. 66, International Commission on Radiological Protection, Elsevier Publ., Tarrytown, NY, 1994;

traffic than adults. As documented below, the overall exposures of children to several motor vehicle-related TACs is not significantly different from adults.

Response 5: Again, the purpose of the draft OEHHA report is not to criticize the language of the statute. However, we do indeed discuss in the draft report the fact that children spend more time outdoors than adults after infancy, and moreover they are generally more active. While that pattern may have changed (but we are unaware of data showing this), it is unlikely to have changed to the point that adults are more active and spend more time than kids outdoors.

Comment 6: The document should discuss claims that: <u>air pollution is known to exacerbate asthma and may be a trigger for asthma attacks in infants and children.</u> This claim is used to support the need for greater protection of the approximately 500,000 children with this chronic disease in California. However, meetings of international experts[3] repeatedly conclude that while high levels of inhaled pollutants may aggravate symptoms or exacerbate the disease, air pollution has no role in asthma etiology. The multi-factorial etiology of asthma is more determined by wide familial, infectious, allergenic or socioeconomic and psychosocial influences. The precipitating factors include primarily allergens (e.g. house mites and molds), respiratory infections and indoor tobacco smoke that affect asthma more than ambient air pollution.[4] The sensitivity of asthmatics is, also, not equal for all air pollutants. For example, asthmatics are more sensitive (i.e. respond with more symptoms) to the effects of sulfur dioxide (SO_2) than the general population. In contrast, reports about asthmatic's sensitivity to ozone are inconclusive, and a low degree of response is reported for particulate matter. It should be emphasized that exacerbation of asthma attacks is always connected with short episodes of high exposures to irritative pollutants and has never been associated with chronic exposures to low levels of air toxics. Consequently, acute exposures from high indoor levels or from peaks during outdoor air pollution episodes may be of concern for asthma exacerbation. However, no

[3] "Asthma and the Environment," Meeting Report by Koren, H.S. and Utell, M.J., NHEERL, U.S. EPA, 1997;

evidence exists that chronic exposure to low levels of toxic air pollutants may produce or aggravate asthma attacks in infancy and childhood.

Response 6: Again, the purpose of the draft OEHHA report is not to criticize the language of the statute. However, in response to the comment, OEHHA staff agree that existing data are inadequate to confidently link air pollution to the etiology of asthma and that the sensitivity of asthmatics is not equal for all air pollutants. However, air pollution is known to exacerbate asthma in those who have the disease. As discussed in the draft report, on a population-wide basis, children have higher prevalence rates of asthma than do adults. In addition, asthma episodes tend to be more serious in children resulting in more hospitalizations of children (particularly from age 0 to 4 years) than of adults. Therefore, on a population-weighted basis, children are more impacted by asthma than adults. More importantly, acute exposures to air pollutants are not the only concern for the exacerbation of asthma. It is true that the statistical power of epidemiologic studies is limited when trying to identify effects of low level exposures to air pollution. Yet even a 1 or 2% increase in the incidence and/or severity of asthma attacks would be a considerable and costly health problem in asthmatic children. Air pollution can potentially result in exacerbation of asthma for hundreds of children in a large metropolitan area, regardless of whether air pollution caused the disease in the first place.

Comment 7: The document should discuss claims that: <u>infants and children's developing organs and tissues are more susceptible to damage from some environmental contaminants</u>. Except for lead, this argument is very weak; the document should clearly state that evidence for these effects is extremely scarce. When reported, the effects are produced solely by high pollutant concentrations that are not relevant to low ambient concentration of air toxics.

Response 7: Again, the purpose of the draft OEHHA report is not to criticize the language of the statute. In response to the comment, OEHHA is aware that in many cases

[4] "Asthma Death Rates in the United States by Race, Age and Year between 1980 to 1993", U.S. MMWR, 1996;

the evidence for differential sensitivity is preliminary or partial, and has attempted to characterize such evidence appropriately in the draft document. However, on examination of the scientific literature it appears that there are several examples of reliable evidence for such effects, and that these cases are not confined to lead, nor to high levels of exposure.

Comment 8: These generalized arguments, on which the disproportionately higher susceptibility of infants and children to air toxics is postulated, do not provide a satisfactory scientific basis for TAC prioritization. Even if these highly protective public health views are accepted, the document should inform the reader with a full and balanced description of the uncertainties that are involved in these decisions.

Response 8: Once again, the commenter is referring to the language in the statute, which OEHHA did not write and is not charged with either defending or criticizing. In response to the comment, OEHHA has not used generalizations without additional evidence to list TACs "that may cause infants and children to be especially susceptible to illness" pursuant to Health and Safety Code Section 39669.5(a). OEHHA has attempted in the draft report to make clear the distinction between clear evidence and preliminary evidence or standard assumptions. Some specific cases where this attempt was insufficiently successful have been identified in responses to specific comments and will be addressed in the final version of the document. It should be noted that the general considerations addressed in the immediately previous comments are by no means the only basis for the conclusion that some TACs may have differential impacts on infants and children. Indeed, many of those TACs assigned higher priority in OEHHA's document received that rating because specific experimental or epidemiological data exist which tend to support the existence of a differential effect. Agents where the conclusion is based solely on general arguments generally received lower priority ratings.

II. Methodology for prioritizing TACs

Comment 9: The limitations of the existing data and knowledge concerning greater susceptibility of infants and children are such that there is no obvious or clear-cut methodology to use in prioritizing TACs under SB 25. The draft indicates that OEHHA staff developed a system for prioritization. First, over 200 TACs were ranked by the ratio of their ambient concentrations divided by their chronic Reference Exposure Levels (RELs). Next, carcinogens were ranked by their unit risk times the ambient concentration. Third, the two lists were combined. It is acknowledged that this ranking did not include any information on differential sensitivity of infants and children.

Next, a list 34 TACs was chosen for focused literature reviews. The draft indicates that the list was developed in part from the ranking noted above, in part from the "known toxicological endpoints of the chemicals," and in part from California emission data. Based on the focused literature reviews, eleven potential candidates for listing of Toxic Air Contaminants that "disproportionately impact infants and children" were chosen.

The process for choosing 11 compounds from the list of 34 TACs chosen for focused literature reviews is unclear. The draft indicates that "the decision was heavily influenced by the toxicity of the compounds and less so by the estimated exposures to the compounds." However, "toxicity" or risk does not exist independent of the dose of the substance.

The draft indicates that OEHHA staff used the following criteria as a guide for prioritizing the contaminants: (1) any evidence that children may be more susceptible to the effects of air contaminants than adults; (2) the nature and severity of effects, especially irreversible effects in children; (3) any indication that the existing health criteria may not be adequately protective of children; (4) any potential difference in children's susceptibility to carcinogenesis by these compounds; and (5) the extent of exposure to and magnitude of the risk from these compounds at ambient California concentrations. However, there is no indication as to how these various criteria were

measured or weighed. Thus, there is no indication of why the five substances proposed for Tier 1 were chosen other than the discussion on pages 6 and 7. OEHHA should make the various rankings and the complete list of 34 substances public to aid the reviewers of the draft.

Response 9: OEHHA thanks the Alliance for their summary of the procedures used. Further nuances may be glimpsed by reading the account in the OEHHA draft document, and also in our response to several other commenters who expressed an interest in the prioritization process used.

Unfortunately the timetable imposed on OEHHA by the legislation does not allow for further public comments to be submitted at this stage. However, OEHHA will be happy to share additional information with interested parties.

We should note that there were 35, not 34, chemicals for which focused literature reviews were conducted.

Comment 10: Clearly, a great deal of professional judgement went into the prioritization. However, it is not clear who on the OEHHA staff participated or how the final decision was made.

Response 10: OEHHA has attempted to explain the process as clearly as possible, but agrees that in view of the considerable uncertainties and deficiencies in available data a considerable element of scientific judgment was necessarily involved in the final decision.

OEHHA draft reports are the subject of intensive internal peer review and management review prior to their publication, and are issued in the name of (and with the support of) the Director of OEHHA. Although contributing authors are sometimes acknowledged for professional reasons, it has not been OEHHA policy to identify individual staff who

participated in specific decisions, nor is it clear why the commenter would be interested in such information.

Comment 11: We have the following concerns with the methodology: First, the initial ranking and combination of rankings did not consider either the differential sensitivity of children or the likelihood that the basis for the TAC listing has any relevance to infants or children. To identify potential TACs of concern to children without consideration of why that pollutant was initially determined to be a TAC by California ignores a great deal of fundamental science and knowledge that should enter into the determination. An example of this concern is provided in the specific comments on diesel exhaust particulate.

Response 11: The initial prioritization was in the case of many less studied TACs constrained by the lack of any specific data relating to infants and children, or younger life stages of experimental animals. The draft document explains (page 3-4, paragraph IIA.4 of the introduction) that where data specific to infants and children, or other material information, were available, these were considered in addition to the numerical ranking process described. The example of diesel exhaust is one where such additional inputs were available and were important in the overall prioritization process for that TAC.

Comment 12: It is not clear why OEHHA used the ambient air concentrations rather than estimates of actual personal exposure to rank substances. Since people spend the vast bulk of their time indoors, the risk from highly reactive TACs that do not penetrate indoors will be overestimated if only the ambient concentration is used. Similarly, for TACs with substantial indoor sources, use of the ambient concentration will underestimate the risk. Therefore, the literature reviews for the 34 substances need to discuss and evaluate penetration into indoor environments, particularly homes and schools, as well as indoor sources and levels.

Response 12: The Children's Environmental Health Protection Act amends the enabling regulations of California's Toxic Air Contaminants program. At the present time these regulations do not include any broad regulatory powers relating to indoor air. Therefore the overall intent of the prioritization process was directed towards outdoor air pollutants, although OEHHA has not ignored the contribution of indoor exposures when assessing the current impact of certain pollutants. It should be noted that the TAC program does address both general ambient levels in outdoor air and also hot spots resulting from localized emissions. Furthermore, the data on "actual personal exposure" are extremely limited for the TACs, and so would not be particularly useful. In contrast, the Air Resources Board has amassed years of data measuring specific compounds in ambient air.

It must also be realized that Californians enjoy year-round mild weather in most areas of the state and windows are open frequently. The models, which are most relied upon in describing lower concentrations of ambient air pollutants outdoors compared to indoors, do not inform adequately when the windows are open. Furthermore, measurements of certain pollutants indoors and outdoors do not show much protection (e.g., fine particulate matter) by shutting up a house. In addition, some of the compounds that are TACs have indoor sources and these are a concern.

Comment 13: For some TACs there are also significant body burdens due to intake in food and water. Therefore, the literature reviews for the 34 substances need to evaluate all exposures and whether the route of exposure makes a difference depending on fate of the substance in the body. The U. S. EPA's Cumulative Exposure Project is currently estimating 37 contaminants in 34 foods, including different age sub-groups. The results are expected soon. This significant database should be helpful in the prioritization.

Response 13: OEHHA is familiar with US EPA's Cumulative Exposure Project, and looks forward with great interest to the outcome both of this project and of some parallel activities currently being undertaken by California agencies. However it should be noted that, as emphasized in the response to the previous comment, the current activity is

directed specifically to airborne pollutants covered by the Toxic Air Contaminants program. Furthermore, some compounds, e.g., dioxins, are initially airborne, deposit on food and feed and enter the food chain. Controlling airborne sources thus reduces overall exposures.

Comment 14: The REL, by definition, is already a concentration that includes highly conservative margins of safety to protect the most sensitive individuals in the population. These corrections compensate for unresolved uncertainties in the risk assessment methodology and already include highly susceptible or sensitive individuals, i.e. those with increased exposure (incl. **children**) and those undergoing greater physiological change (incl. **children).** That means that the RELs already account for the alleged susceptibility of infants and children by including large multiplicative margins of safety that range up to 3,000. The REL, therefore, cannot properly be used to identify candidates "producing disproportionately higher effects in children."

Response 14: OEHHA and California or US regulators have previously operated on the assumption that the commenter's assertion that existing standards are protective of children is true. However, various scientific and policy analysts have become concerned that this assumption is not supported by sufficient evidence, hence the present legislation and the process it mandates. The fact that the REL was not the exclusive input to the initial phase of prioritization has already been addressed in comment II.3. Use of the REL gave a general indicator of the proximity of measured ambient air concentrations to a potential level of concern, and thus was a useful yardstick in comparing one TAC with the next.

Comment 15: The screening analysis to identify potential TACs used metrics that involve lifetime exposures. For example, chronic RELs are developed to protect for a full lifetime of exposure including potential periods of increased susceptibility during childhood. Similarly, cancer unit risks for individual TACs are developed and adopted assuming 70yr-long exposures. These characteristics make the RELs or cancer unit risks inappropriate for assessing risks during the much shorter exposure periods of infancy and

childhood. Certainly, they do not provide any information on the question of whether or not exposures during childhood are more important for irreversible effects or cancer developments than exposures during the rest of the lifetime.

Response 15: Firstly, exposure to some toxic agents early in life can carry increased lifetime risks (e.g., some carcinogens). Secondly, developmental toxicology endpoints, which were the basis of some of the RELs, are often irreversible, thus impacting the organism or person for their entire lifetime. Endocrine disrupting chemicals may also have the potential to have long-lasting effects after short early-life exposures. Thirdly, it is important to note that chronic RELs are not restricted to lifetime exposures; instead they represent long-term exposures up to a lifetime. As indicated in our chronic REL document human exposures for eight years or longer were not adjusted to a lifetime exposure. In order to comply with the SB25 statute in the mandated time frame, we prioritized on the basis of existing assessments. Furthermore, that is the reason we did not rely solely on that initial prioritization and why we perused the entire TAC list to make sure that we had not missed an obvious candidate for listing. As noted in the draft report, because of this, the compounds were not prioritized solely on this basis.

OEHHA used data that were available in its consideration of the TACs at each stage of prioritization. Unfortunately for some agents only adult toxicity data are available. In most, but not all, cases adult toxicity is the basis of the REL. Some RELs use developmental endpoints, and some TAC identification documents do include consideration of data on young animals or infants and children when these were available. The fact that the REL or cancer potency was not the exclusive input to the prioritization has also been addressed in comment II.3.

Comment 16: Because risk assessment approaches are completely different between respiratory irritants and documented human carcinogens, it would seem more appropriate to prioritize and rank TACs separately for non-cancer hazards and for carcinogenicity. The prioritization of non-cancer hazards is conceptually similar to traditional approaches to threshold-possessing chemicals (as identified by inhalation reference concentrations

(RfC) or Reference Exposure Levels (REL)) while the assessments of potential carcinogens use lifetime exposure-predictive cancer unit risks. Not only is there a large uncertainty inherent in these lifetime risk estimates (frequently derived from animal experiments), but the assessment also presumes a lifetime-long exposure to predict the possibility of tumor generation. Because we do not know whether or not infancy or childhood exposure represents a more sensitive period of life for cancer induction or whether contact with a cancer-inducing chemical during early childhood can predispose for irreversible effects formation, it would be appropriate first to determine the increased susceptibility of children for non-cancer health effects.

Response 16: OEHHA sympathizes with the commenter's view that the cancer and non-cancer endpoints are difficult to compare (although note should be taken of recent efforts to facilitate such comparisons, as described in the US EPA's recent drafts of the revised Carcinogen Risk Assessment Guidelines and in some recent carcinogen risk assessments by OEHHA). However, the wording of the legislation specifies a single list and therefore requires OEHHA to make such a comparison by the best available means.

OEHHA has identified several instances where compound specific data exist suggesting or demonstrating enhanced sensitivity of fetal young animals or humans to carcinogens (see for more detail the summaries on vinyl chloride, benzene and benzo[*a*]pyrene). The comment appears to imply that tumors can only arise, or the rate of incidence be predicted, after lifetime exposure to carcinogens, not shorter periods. While cancer potencies are normalized to a 70-year exposure for the sake of standardization and comparison, it does not follow thay can only produce cancer after 70 years of exposure. California risk assessment guidelines specify default assumptions for developing risk estimates from experimental exposures less than the standard lifetime of the exposed species. In addition, Dr. Ed Calabrese has compiled a database of carcinogens that increase tumor incidence after short-term exposures. In view of these findings, the more general considerations addressed in the document introduction, and the substantial impacts of carcinogenic pollutants on public heath, it seems inadvisable and contrary to

the legislative mandate to ignore or defer consideration of these agents for differential impacts on infants and children.

Comment 17: Since other than purely genotoxic mechanisms may be involved in tumor generation and the significance of non-genotoxic mechanisms such as chemically induced cell proliferation (Butterworth et al., 1991[5]) has not yet been definitively established, the possibility exists that the tumor-producing chemicals may also have verifiable no-effect levels. This introduces an additional uncertainty into the ranking of potentially carcinogenic toxic air contaminants. The reasons that all cancer-producing air toxics are evaluated in the document on the basis of assumed genotoxicity should be discussed in the document and the levels of uncertainty this introduces should be emphasized.

Response 17: OEHHA has addressed some specific aspects of carcinogenic mechanisms applicable to individual TACs in the toxicity summaries. These issues were discussed to the extent that the information was available in the original TAC documents. California has already addressed the general issue of genotoxic and epigenetic ("non-genotoxic") mechanisms in earlier guideline documents and risk assessments.

Comment 18: Because of these concerns, it is not clear that OEHHA ended up with a list that is responsive to the legislative mandate. It may be a list of the most important TACs, the most important TACs based on ambient exposure, or the most important TACs that also "may" have differential effects. However, it is not clear that it is a list of TACs that "may cause infants or children to be especially susceptible to illness." We recommend revising the literature reviews as suggested above and re-evaluating the results based on total personal exposure. Another approach would be to rank TACs solely on the evidence for greater susceptibility of infants and children. If the various approaches identify the same substances, OEHHA and ARB will have greater confidence that the list fulfills the legislative mandate.

---

[5] "Chemically Induced Cell Proliferation: Implications for Risk Assessment", Eds.: Butterworth, B.E., Slaga, T.J., Farland, W., McClain, M., Wiley-Liss, Publ., New York, N.Y., 1991;

Response 18: OEHHA believes that the public review draft represents the best response to the legislative mandate given the data available and the required timetable. However, OEHHA looks forward to incorporating any substantive improvements identified during review of the public comments and discussions with the Scientific Review Panel.

III. In addition, OEHHA staff should consider the following in finalizing the TAC rankings:

Comment 19: The progress in reducing motor vehicle-related TACs should be documented in the report.

Because of the on-going motor vehicle and fuel control program in California, the emissions and, therefore, ambient concentrations of the motor vehicle-related substances discussed in the report have been decreasing for several decades and will continue to decrease for the next several decades. The interpretation of the significance of epidemiological studies, emission inventories, and reported ambient measurements all need to be informed by this continuous improvement. OEHHA indicates that the prioritization depends in part on "the extent of exposure to and magnitude of the risk from these compounds at ambient California concentrations." Where these exposures and risks have been declining and are forecast to continue to decline, this fact needs to be documented.

For example, EPA recently completed its Motor Vehicle and Motor Vehicle Fuel Hazardous Air Pollutant Rulemaking. EPA projected emissions and toxic exposures assuming implementation of Phase II reformulated gasoline, the National Low Emission Vehicle (NLEV) program, Tier 2 emission standards with 30 ppm sulfur gasoline, 2004 Heavy-duty standards and 2007 Heavy-duty standards. The agency concluded:[6]

[6] U. S. EPA, Technical Support Document (TSD): Control of Emissions of Hazardous Air Pollutants from Motor Vehicles and Motor Vehicle Fuels, EPA420-R—00-023, December 2000, at page 125

"With these controls, by 2020 we expect that inhalation exposure to benzene attributable to on-highway vehicles will decrease from 1990 levels by 74 percent, exposure to formaldehyde by 75 percent, exposure to acetaldehyde by 65 percent, exposure to 1,3-butadiene by 73 percent, and exposure to diesel PM by 93 percent."

In California, similar detailed calculations have not been carried out. However, there are projections of reductions in Reactive Organic Gases that can be used to estimate the magnitude of the reduction in toxic gases expected from the control programs currently in place. Projections of the reduction of Reactive Organic Gases (Ozone Inventory, in tons per day) in the South Coast Air Basin from the current motor vehicle control program with EMFAC20000 (version 2.02) indicate the total ROG from gasoline and diesel vehicles will be reduced by 72 percent from 2000 to 2020. The reduction in gasoline exhaust ROG from 2000 to 2020 is projected to be 83 percent. Thus, the reduction in motor vehicle-related TACs in California will continue for the next several decades.

Response 19: The present stage of the process is concerned with identifying TACs for placement on the list, based primarily on toxicity information and secondarily on evidence for current exposures in California. Data on specific sources of the materials or trends in emissions are not therefore part of the input at this stage, but will undoubtedly be of great interest to the California Air Resources Board when it reconsiders the requirements for Air Toxics Control Measures. Furthermore, reductions in motor vehicle pollution, while very important, have not eliminated urban air pollution.

Comment 20: Recent EPA analyses document that children's exposure to ambient TACs is the same as the general population's exposure.

As part of the recent EPA rulemaking on hazardous air pollutants, the Agency analyzed inhalation exposures with a new version of the HAPEM model the Agency used in its 1993 Air Toxics Study. The model simulates the movement of individuals between home and work and through a number of different microenvironments. The model links human

activity patterns with estimated ambient concentrations to develop average exposure estimates for 22 different demographic groups and for the total population.

Part of the analysis was aimed at evaluating groups, outdoor workers and children, that were thought to experience higher than average exposure. However, the Agency concluded:[7]

> "We have analyzed average inhalation exposures for three demographic groups—the overall population, outdoor workers, and children 0 to 17. Since inhalation exposures to air toxics from outdoor sources are typically lower indoors than outdoors, exposures for outdoor workers are somewhat higher than the general population. Exposures for children are similar to the general population, although slightly lower since children spend a little more time indoors than most other demographic groups."

Response 20: OEHHA thanks the commenter for bringing this report to their attention. It will receive detailed consideration during subsequent phases of the evaluation, along with other findings and opinions on the topic, not all of which reach similar conclusions. In addition, the EPA report was only addressing exposure in a limited sense as the concentration at the boundary of the organism. This does not include considerations of higher ventilation rates per unit body weight and the influence on absorbed dose.

Comments on specific substances

Comments on Specific Substances - Benzene

Comment 1: Benzene is characterized in the document as a human carcinogen (USEPA, 1998) based on epidemiological studies of increased incidence of acute myeloblastic leukemia in high occupational exposures. However, the chronic toxicity of occupational exposures first produces effects on bone marrow and formation of blood cells prior to the

induction of leukemia. Therefore, the question of whether the actual carcinogenic action of benzene is due to the genotoxic effect of benzene and its metabolites or whether the leukemogenic action is due to an induced secondary cell proliferation in response to repeated hematotoxic insults has not yet been resolved (OEHHA, 2000, HEI 1999[8]). These aspects of benzene carcinogenicity should be discussed in the document because they are crucial for a correct assessment of the effects of low level ambient exposures. If the non-genotoxic character of benzene requires that repeated hematotoxicity precede the leukemogenicity, the carcinogenic effects cannot be produced by low exposure and are expected to show, similarly as other toxic effects of benzene a discrete no-effect (threshold) level.

This has raised important policy questions that HEI and others are investigating:[8] Is benzene hematotoxicity a necessary stage in development of leukemia? Does leukemia from benzene have a threshold? Because assessing the risk to infants and children or the general population requires extrapolating from occupational exposures in the ppm range to ambient exposures in the ppb range, the OEHHA report should acknowledge the possibility that benzene toxicity may have a threshold and, therefore, that the use of linearly extrapolated cancer unit risks may be inappropriate.

Response 1: The current document is not a risk assessment document nor is it a discussion of the benzene quantitative risk assessment conducted under the Toxic Air Contaminant program. Benzene is a genotoxic carcinogen and is treated as a non-threshold carcinogen by both the U.S.EPA and Cal/EPA. We believe linear extrapolation is appropriate.

Comment 2: The text should also recognize that benzene hematotoxicity as well as the developmental and reproductive effects require exposures to concentrations much higher than those found in ambient air in California. The use of Relative Exposure Levels (REL) based on occupational exposures (Tsai, et al., 1983) is inappropriate for the listing

[7] December 2000 TSD at page 121.
[8] "Research on Air Toxics, Health Effects Institute Program Summary, May 1999.

of benzene because chronic RELs already use a margin of safety (uncertainty factor) to account for more susceptible subpopulations, including children. (OEHHA, 2000)

Response 2: The Reference Exposure Levels (REL) available for the TACs were used during the prioritization in order to see which chemicals have ambient air levels close to a level of concern. Thus, they were used in a comparative sense. While it is true that the REL is determined by using uncertainty factors which we assume are protective, we are embarking on an evaluation of whether the risk assessment methods are adequate to protect infants and children.

Comment 3: The use of gasoline and mobile source–related emissions have been traditionally considered as the largest sources of outdoor benzene emissions (highway vehicles, 48 % and all mobile sources 76%, National Toxic Emissions Inventory, 1996), and benzene-containing environmental tobacco smoke has been estimated to account for 50 % of human exposure in the U.S. (Wallace, 1995).

However, there have dramatic reductions in ambient benzene in the last four decades. Singh, et al[9] report benzene concentrations in 12 U. S. cities during 1979 and 1984. They report background concentrations in remote locations and summarize the available trend data for benzene in the South Coast Air Basin from 1960 to 1983, concluding that benzene and toluene declined by a factor of 5 to 10 over the period studied. For benzene, the ambient concentrations were reduced from 15 to 40 ppb in the 1960's to 2 to 5 ppb in the early 1980's. Fruin, et al.[10] have recently documented a 70 percent reduction in ambient benzene between 1989 and 1997. Consistent with this data, the OEHHA draft indicates that 1982 levels were roughly 5 ppb and 1997-99 levels were 0.85 ppb. Thus, there has been a reduction of between 95 and 98 % in ambient benzene concentrations in California since the 1960's. As documented in the General Comments above, the progress in reducing ambient benzene exposures from motor vehicle emissions will continue through at least 2020.

[9] H. B. Singh et al, "Distrtibution of Aromatic Hydrocarbons in the Ambient air, " Atmos. Env., **19**, pages 1911-1919 (1985).

[10] S. A. Fruin, et al., "Reductions in human benzene exposure in the California South Coast Air Basin," Atmospheric Environment, **35**, pages 1069-1077, 2001.

One of the major concerns noted in the draft is that benzene causes childhood or adult onset leukemia. If ambient benzene is a major or significant cause of adult leukemia, the build-up of benzene in the 20's, 30's, 40's and 50's due to increased gasoline use and now its reduction due to emission control should be reflected in myeloblastic leukemia cases. National health statistics show that the U.S. mortality due to myelogenic leukemias did not change between 1950 and 1979 in spite of the fact that annual gasoline consumption increased dramatically over the past decades.[11]

Similarly, if ambient benzene is a major or significant cause of childhood leukemia, the dramatic reductions in ambient benzene in the last 40 years should have resulted in a reduction in childhood leukemia. However, as noted in the draft, childhood leukemia is actually increasing slightly. Importantly, the implications of benzene as a potential risk for the development of leukemia in children cannot be accepted because the type of leukemia (primarily acute lymphocytic leukemia) found in children was not found among the occupational benzene-induced myelogenous leukemias. Their attribution to paternal and in utero exposures to ambient benzene concentrations (OEHHA, 1997) is questionable and should be rejected in the present document. Animal studies on developmental and reproductive effects of benzene (OEHHA, 1997, 2000) were conducted with exposures that cannot be compared with low ambient concentrations, are expected to have clearly defined thresholds, and are irrelevant to the assessment of ambient exposures. We concur that "there are no human studies available that have examined childhood exposures to benzene and increases in lifetime risk of cancer" (OEHHA, 2001, benzene, page 4).

Response 3: Reductions in ambient benzene concentrations have resulted primarily from regulatory efforts on the part of the California Air Resources Board and OEHHA. Cancer risks from benzene based on our linear extrapolation model are still above acceptable levels in urban areas. However, the risk estimates are below those that would be detectable even in a large epidemiology study from ambient exposures alone. Thus,

[11] "U.S. Cancer Mortality Rates and Trends, 1950-79", NCI/USEPA, EPA-600/1-83015a, September 1983;

leukemia rate measurements, which reflect all causes of leukemia, are not a good metric to assess the value of reductions in benzene or the contribution of benzene to all leukemias.

Comments on Specific Substances – Dioxins

Comment 1: The U. S. EPA has been preparing a risk assessment for dioxins for several years. As noted in the OEHHA draft, EPA developed detailed emission inventories for 1987 and 1995 indicating that nationwide dioxin emissions were reduced by 75 % over that time frame. While leaded-gasoline vehicles emitted some dioxin due to the chlorine in the lead scavengers, the switch to [un]leaded gasoline and catalytic control systems has essentially eliminated gasoline exhaust as a source of dioxin. EPA's inventory indicates that unleaded gasoline vehicles are responsible for less than 0.2 percent of the dioxin released to the environment in 1995. Based on a recent tunnel study, EPA has estimated that diesel vehicles are responsible for the order of 1 percent of nationwide dioxin emissions. With the diesel control program in place federally and in California, the major reductions in diesel exhaust particulate should reduce the diesel's contribution to dioxin by about a factor of ten over the next twenty years.

The U. S. EPA's Science Advisory Board (SAB) has been reviewing the EPA Dioxin Reassessment. In mid-March, the SAB posted a draft report on its web site that has extensive discussion of the many scientific questions surrounding dioxin risk. We recommend that OEHHA consider the material in the SAB draft (and final report when it becomes available) as well as the material in EPA's risk assessment in its deliberations.

Response: **1** OEHHA is continuously searching the scientific literature on priority chemicals. USEPA's reports are only one of its sources of information, but one that is taken very seriously. We are familiar with their draft report on dioxin and related compounds, including their inventory calculations. The draft report contains information that supports the listing of dioxin as a TAC that may cause infants and children to be especially susceptible to illness. We also await with interest measurements currently being made or planned by US EPA, and by various agencies in California, which may further clarify the sources, environmental distribution, and fate of dioxin-like contaminants. If the draft prioritization is confirmed, these data will obviously be important in the Air Resources Board's consideration of possible modifications or additions to their Air Toxics Control Measures.

Comments on Specific Substances - Formaldehyde

Comment 1: As discussed in the General Comments above, the motor vehicle control program is reducing formaldehyde. Even though ambient formaldehyde is both a direct emission and a product of photochemical reactions of hydrocarbon emissions, a continuing reduction in both primary and secondary formaldehyde is projected. Unfortunately, the trend in ambient formaldehyde is not as well documented as for other TACs, in part because of problems with ARB's measurements in the early and mid 1990's that were not discovered until some time later. However, ARB's recent data documents that statewide ambient concentrations in 1998 averaged 2.7 ppb. This is in contrast to the indoor concentrations that are reported in the draft to average 24 ppb for office and public buildings, 50 ppb for conventional homes, and 72 ppb for mobile homes.

Response 1: We agree that indoor concentrations can be much greater than the average statewide ambient concentration and are concerned about indoor formaldehyde exposures.

Comment 2: As noted in the draft, the chronic REL is 2 ppb based on symptoms of irritation in workers, and the acute REL is 74 ppb based on irritation of asthmatics. The draft indicates formaldehyde was chosen as a Tier 1 TAC in part because the chronic REL is below urban and indoor levels and in part because of exacerbation of asthma. Just because an exposure exceeds a REL doesn't necessarily indicate a risk or problem. EPA indicates that estimated concentrations greater than health benchmarks should be viewed as an indicator of a potential public health problem and not as characterization of actual health risk.

Response 2: In California, the chronic REL is selected to designate a concentration below which people will be safe from toxic effects. Chronic exceedances of this

concentration should be regarded as cause for concern. We agree that an exceedance of an REL is not automatically associated with a health impact. The RELs were compared to the measured ambient concentrations to help us prioritize which substances might be close to levels of concern and which are not. That criterion was only one piece of information that came into play.

Comment 3: Since even the peak ambient levels are significantly below the acute REL, there is no evidence that ambient formaldehyde contributes to exacerbation of asthma. With the continuing reduction in primary formaldehyde emissions as well as the hydrocarbon emissions that produce secondary formaldehyde in atmospheric reactions, the focus of OEHHA's analysis should be on indoor formaldehyde levels that can reach 500 ppb according to the draft.

Response 3: We agree that indoor sources of formaldehyde are a significant problem. The OEHHA report is neither a risk assessment nor a risk management report. Rather it is a hazard identification report. The listing of a substance on the SB 25 TAC list triggers the Air Resources Board to look at their existing control measures or the need for one if one does not exist. At that point ARB needs to decide what can be done to control sources of formaldehyde whether indoors or out. Krzyazanowski et al. (1990) found greater prevalence rates of asthma in children from houses with formaldehyde concentrations greater than 60 ppb. They also found that in formaldehyde concentrations below 50 ppb, peak expiratory flow rates in asthmatic children were less than in healthy children. Both these findings suggest at least exacerbation of asthma by formaldehyde. Consideration of concentration and toxicity applies whether the exposure is inside or outside.

Comment 4: The other endpoint of concern with formaldehyde is cancer. Since the risk assessments conducted by both EPA and OEHHA, new research has been conducted concerning the occurrence of respiratory tract tumors in rats. In addition, a new biologically-based dose-response model has been developed. The new model is being

used to revise the current EPA cancer potency estimate. A draft assessment is expected to be ready for SAB review in Spring 2001.[12] OEHHA should review the new material and, after SAB review, update the California unit risk as appropriate.

Response 4: We appreciate the comment and are following the work being done on formaldehyde with interest. However, since the OEHHA draft report is not a risk assessment document, the comment is not germaine in this context.

[12] EPA TSD, December 2000, page 66.

Lead

Comment 1: There has been a dramatic reduction in ambient lead over the past 40 years due to the phase out and elimination of lead in gasoline. Over the 1960-1965 period… lead concentrations…averaged 3.1 $\mu g/m^3$ at residential sites, 6.8 at commercial sites, and 7.8 at freeway sites. When these levels are compared to the state-wide ambient lead level of 0.014 $\mu g/m^3$ in California in 1999, it is clear that near-ground ambient lead concentrations have been reduced by over 99.5 percent since the early 1960's.

Response 1: OEHHA acknowledges the dramatic decrease in ambient lead levels since the 1960's. However, while lead levels in air and blood have been dropping, it has not been possible to demonstrate a threshold blood lead level below which there are no adverse effects. In addition, air lead levels in the vicinity of stationary sources of lead emissions can be significantly higher than ambient levels. OEHHA considered this fact in the context of the demonstrable adverse effects of lead when making its tier assignments.

Comments on Specific Substances – Benzo(a)pyrene and other Polycyclic Aromatic Hydrocarbons

Comment 1: Because benzo(a)pyrene and some other PAHs are considered human carcinogens, concerns about the tumor producing effects of these complex mixtures dominate the discussion of the need for additional protection of infants and children. However, there is no evidence that infants or children would be more susceptible to these compounds at ambient exposures than adults. Animal studies used in support of these claims (Perera, 1998, LaVoie, 1994) use extremely high concentrations of dissolved hydrocarbons administered into the organism and ignore the question of the bioavailability of particle-adsorbed PAH and the extremely low levels inhaled under ambient conditions. Scientific data that address the release of the adsorbed hydrocarbons in vivo and deposited doses under ambient conditions are discussed below in connection with the carcinogenicity of diesel particulate. The data indicates the results of the high concentration animal experiments are not relevant for present ambient conditions and that extrapolation to low ambient concentrations is inappropriate. The same criticism applies also for field observations where adverse reproductive effects observed in humans are indiscriminatively attributed to PAHs (Perera, 1998, Sram, 1996, 1999) without excluding the role of other confounding factors.

Response 1: In the toxicity summary for benzo[*a*]pyrene and other PAHs OEHHA identified not only carcinogenicity but also various other toxicological end-points including developmental toxicity and immunotoxicity. It is certainly true that the consideration of adult toxicity of PAHs tends to be dominated by the carcinogenic effects, but this is not necessarily true for consideration of differential impacts on infants and children.

The assertion that "there is no evidence that infants or children would be more susceptible to these compounds at ambient exposures than adults" is based on the subsequent attempt to discount the considerable evidence (some of which was briefly cited in OEHHA's toxicity summary) tending to support the opposite view. OEHHA is well aware of the concerns and difficulties in extrapolating between routes of exposure and from high to low doses for PAHs, and these matters received considerable attention

in the TAC document on benzo[*a*}pyrene (OEHHA, 1993; Collins et al., 1998; cited in the draft toxicity summary). OEHHA does not consider that these concerns provide grounds for dismissing the available experimental data as proposed by the commenter. In the case of PAHs, there are specific experimental and epidemiological grounds for expecting that extrapolation of experimental data to actual human exposure situations is reasonable, in addition to the policy defaults which mandate such extrapolation in the absence of clear evidence to the contrary. It should also be noted that the human PAH exposures of concern under the Toxic Air Contaminant legislation are not confined to "background" ambient levels, but also include hot spots and other special situations where exposure may be much higher.

OEHHA notes the concern of the commenter about confounding factors in the studies by Perrera, Sram and others. These reservations and limitations were also noted and discussed by the authors and other commentators in the scientific literature, but OEHHA nevertheless considers that these findings shed important light on the role of PAHs in pollution-related human health effects. This belief is supported by the finding of DNA adducts associated with PAHs in studies of mothers and infants exposed to polluted air (for example, Whyatt et al., 1998, cited in the draft toxicity summary)

Comment 2: Currently, the EPA inventories PAHs with a measurement that is the sum of 7 carcinogenic PAHs. In the 1996 National Toxics Inventory, EPA attributed 4 percent of total national PAH emissions to highway motor vehicles and an additional 2 percent to nonroad mobile sources.[13]

There have been dramatic reductions in benzo(a)pyrene and other PAHs from highway motor vehicles during the last 30-40 years. Although the extent of data on BaP and PAH emissions is not large, it is clear that BaP from uncontrolled leaded-gasoline vehicles was significantly greater than that from diesel trucks. It is also clear that emission control devices (the catalytic converter in particular) and reductions in oil consumption have

[13] December 2000 TSD at page 85.

reduced the emissions of BaP and other PAH dramatically. (See Begeman and Colucci,[14] Lang et al,[15] Rogge et al.[16] and Lowenthal et al[17])

Tunnel studies confirm the results from emission studies that individual VOC and PAH have been dramatically reduced from the motor vehicle fleet. For example, Benner, Gordon and Wise[18] measured individual polycyclic aromatic hydrocarbons (PAHs) in the Baltimore Harbor Tunnel in 1985/86 and found levels of several PAH were a factor of 5 to 10 lower than the concentrations measured by Fox and Staley[19] in the same tunnel in 1975. They ascribed the reduction to the use of catalytic converters. Zielinska,[20] et al. have recently presented the results of a new study that included both emission measurements and tunnel measurements. The complete data set will be available soon. It can be used to compare with earlier measurements to document the improvement in PAH emissions.

Ambient measurements also demonstrate that current levels are significantly below prior levels due to controls on motor vehicles and other sources. The summary of BaP content of urban air in Colucci and Begeman[21] can be compared to the recent data from ARB's toxics network to demonstrate the improvement.

Response 2: OEHHA thanks the commenter for providing this information on current automobile-related sources of PAHs. The present stage of the process is concerned with

---

[14] C. R. Begeman and J. M. Colucci, "Polynuclear Aromatic Hydrocarbon Emissions from Automotive Engines, " Society of Automotive Engineers paper # 700469 (1970).
[15] J. M. Lang et al, "Characterization of Particulate Emissions from In-Use Gasoline-fueled Motor Vehicles, " Society of Automotive Engineers paper # 811186 (1981).
[16] W. F. Rogge et al, "Sources of Fine Organic Aerosol. 2. Noncatalyst and Catalyst-Equipped Automobiles and Heavy-Duty Diesel Trucks, "Environ. Sci. Technol., **27**, pages 636-651 (1993).
[17] D. H. Lowenthal et al, "Characterization of Heavy-Duty Diesel Vehicle Emissions, " Atmos. Environ., **28**, pages 731-743 (1994).
[18] B. A. Benner, et al, "Mobile Sources of Atmospheric Polycyclic Artomatic Hydrocarbons: A Roadway Tunnel Study," Environ. Sci. Technol., **23**, pages 1269-1278 (1989).
[19] M. A. Fox and S. W. Staley, Anal. Chem., **48**, pages 992-998 (1976).
[20] B. Zielinska, et al., "Chemical composition of in-use mobile source emission samples," presented at 11th CRC On-road Workshop, March 2001, San Diego, CA.

identifying up to five TACs for development of the list based primarily on toxicity information and on evidence for current exposures in California. Data on specific sources of the materials or trends in emissions are not therefore part of the input at this stage, but will undoubtedly be of great interest to the California Air Resources Board when they reconsider the requirements for Air Toxics Control Measures.

Comment 3: With the reduction in outdoor sources and levels, along with additional reductions from the on-going motor vehicle control program, the focus should shift to indoor sources. The draft documents that there are significant indoor sources. In addition, PAHs in food and its bioavailability should be considered to evaluate the total body burden.

Response 3: Indoor air exposures and food-borne exposures are undoubtedly of great interest to OEHHA. We defer to the ARB regarding the consideration of additional media and routes of exposure when undertaking exposure assessments for regulatory purposes (e.g., under the Air Toxics Hot Spots program), and possibly when establishing control measures and similar regulations for specific media.

[21] J. M. Colucci and C. R. Begeman, Environ. Sci. Technol., **5**, pages 145-150, 1971.

Comments on Specific Substances – Diesel Exhaust Particulate Matter

Comment 1: The inclusion of diesel particles in the list is incompatible with the other TACs because it represents a mixture of a wide array of compounds that varies dependent on exhaust temperature, state and design of the engine, composition of fuel and many other factors. The text not only does not adequately characterize or define this "complex mixture of gases, vapors and particles" but fails to differentiate between the gaseous and solid components of diesel emissions or between their different mechanisms of action (page 1, Table 1). In fact, the list includes TACs evaluated elsewhere in the ranking procedure. The wide list of substances in Table 1 makes it difficult to determine which of the substances may be responsible for any postulated effects. It is not surprising, therefore, that the list of potential effects in children does not identify a specific action of Diesel particulate matter but rather confuses the observed effects with highly non-specific measures of air pollution (e.g.., PM_{10}) in general or with effects of multi-factorial origin (asthma, allergic rhinitis, respiratory symptoms, etc.) without attempting to identify the causal role of diesel particles in these effects.

Response 1: Diesel exhaust particulate has been identified as a Toxic Air Contaminant in California. It is therefore subject to the requiremetns of the Children's Environmental Health Protection Act. The fact that the particles may differ from one source to another is irrelevant to this process and furthermore discussed at length during the identification phase. We are not discussing the merits of identifying diesel exhaust particulate as a TAC in the draft document.

Comment 2: As noted above in the General Comments, it is important to recognize why a pollutant was initially determined to be a TAC by California. Diesel exhaust particulate matter was determined to be a toxic air contaminant based primarily on adult human epidemiology studies of workers exposed to high concentrations of diesel particulate matter over long periods of their working life. In addition to these epidemiology studies, there were also rat cancer studies that showed that when rats were exposed to very high concentrations of diesel particulate matter, on the order of milligrams per cubic meter of inhaled air for their lifetime, they developed lung cancer. Those rats that developed lung

cancer had lungs so coated with black soot the normal clearance mechanisms for the removal of particulate matter were overwhelmed. This lack of clearance and the subsequent toxic effects of the particles was determined to be the cause of the lung cancer. The same effect was seen with massive doses of inert particles.

The point is that the primary evidence for diesel particulate matter being listed as a toxic air contaminant is the result of a reported increase in the incidence of lung cancer in highly exposed workers. Since California completed its diesel TAC listing, additional analyses of diesel risk and exposure have been completed, and the U. S. EPA's Science Advisory Board has reviewed several additional drafts of EPA's diesel risk assessment.

Response 2: SB 25 charges OEHHA with establishing a list of TACs that "may cause infants and children to be especially susceptible to illness". The identifucation of diesel exhaust as a TAC in California was discussed fully in the TAC identification document and during the public comment periods. Furthermore, the comment implies that the only reason the rats in the experimental study developed lung cancer is particle overload. Whether that is true or not for the rodent studies, the mechanism does not apply to the occupational studies in humans.

Comment 3: The first important analysis was carried out by the Health Effects Institute. In response to concerns over varying interpretations of the existing epidemiology, HEI convened a Panel of eminent scientists to thoroughly review and analyze the existing epidemiology studies.[22] The review concentrated on the Garshick railroad workers study and the Steenland study of the trucking industry because these were the only studies that had quantitative estimates of exposure. The Panel carried out additional analyses with the original investigator's data for the Garshick study and concluded the study has very limited utility for quantitative risk assessment. The excess risk among job categories is not consistent with estimated increases in exposure and, within all job categories, the relation of lung cancer risk to duration of employment is negative, strongly suggesting a bias in the study. The HEI Panel's analysis of the Garshick data is consistent with that of

[22] Health Effects Institute, Diesel Emissions and Lung Cancer: Epidemiology and Quantitative Risk Assessment, Health Effects Institute, Cambridge, MA, June 1999.

Crump (both the analyses reported in 1991 as well as additional analyses reported in 1999[23]) and not consistent with that of CalEPA. OEHHA should acknowledge the HEI study and should also acknowledge and discuss the analysis that leads Crump 1999 to conclude that any excess risk for train riders is probably related to lifestyle and not diesel exposure.

Response 3: The issues that the comment raises were all debated extensively during the identification of diesel exhaust particulate as a TAC. They are not directly relevant to the draft document or to the mandates of SB 25. At this point we are not developing a dose-response assessment for infants and children. Furthermore, as noted in our responses to comments, OEHHA disagreed with the Crump analysis and conducted many analyses which indicated a positive dose-response relationship in the Garshick studies. Furthermore, even if one did not use the Garshick cohort study, similar estimates of risk are obtained from other studies, a fact also noted in both our Health Effects Assessment of Diesel Exhaust 1998 document and the responses to comments on that document.

Comment 4: The second important finding is that there are large non-diesel organic carbon (OC) exposures that massively confound the railroad worker, truck driver, and other occupational studies that have been used to implicate diesel particulate as a cause of lung cancer. Heuss has reviewed several new exposure studies and concluded: [24]

> "Five exposure studies that include elemental carbon (EC) as well as organic carbon (OC) measurements have identified significant non-diesel OC exposures in railroad workers, truck drivers, mechanics, dock workers, utility linemen, heavy equipment operators, and workers in truck and diesel engine manufacturing. In addition, efforts to reconstruct past exposures for workers in the trucking industry have established that there were even higher non-diesel exposures of potentially carcinogenic materials for professional drivers and workers in the trucking industry in the past. Such non-diesel exposures are capable of confounding the existing epidemiologic studies of occupational exposure to diesel exhaust

[23] K. S. Crump, "Lung cancer mortality and diesel exhaust: reanalysis of a retrospective cohort study of U. S. railroad workers," Inhal. Toxicology, **11**, pp. 1-17 (1999).

[24] J. M. Heuss, "Comments on EPA's July 2000 Draft Health Assessment Document for Diesel Emissions: The Importance of New Information on the Exposure of Diesel-Exposed Populations," Air Improvement Resource, Inc., Novi, Michigan, 2000.

> The new evidence indicates that the existing epidemiologic studies are really studies of mixed exposures to diesel exhaust together with substantial amounts of potentially carcinogenic materials from other sources. Thus, there is another major factor besides smoking confounding the interpretation of the existing epidemiologic studies. Since the Agency acknowledges that studies that examine several occupational risk factors can contribute little to the evaluation of the carcinogenicity of diesel exhaust, it follows that the Draft's characterization of the human evidence for carcinogenicity as "strong" must be re-assessed. The Risk Assessment must recognize that current "diesel" studies are actually studies of occupational exposure to varying types of particulate matter."

Thus, the current California unit risk overstates the risk and the certainty with which the level of risk from diesel particulate is known. The procedural and substantive validity of the TAC listing is being questioned in California.[25] In addition, the California unit risk has not been accepted at the national level. The U. S. EPA's Science Advisory Board in their December 2000 Review[26] agrees with EPA that the Agency cannot adopt a unit risk at this time. In discussing the epidemiologic database in relation to the Hill criteria, the SAB concluded, "there was general agreement that the dose-response criterion has not been clearly met." The comments of one of the panelists, Dr. Roger McClellan, a former CASAC chair, sum up the situation well. He indicates that the occupational studies suggest risk from diesel particulate matter (DPM) and other exposures, but that we don't know the risk from DPM at ambient levels.

Response 4: The purpose of the current OEHHA draft report is not to identify diesel exhaust particulate as a TAC nor is it to establish the dose-response relationship. These have already been done. The issues raised in this comment have already been debated during the identification phase and are not directly relevant both to the draft OEHHA report and the mandates of SB 25.

[25] Request for Determination with the Office of Administrative Law, Docket #99-026; Apodaca, et al. vs. California Air Resources Board, et al., case #OOCECG10832, pending in Superior Court for the County of Fresno.
[26] Science Advisory Board, Review of EPA's Health Assessment Document for Diesel Exhaust, December 2000.

Comment 5: If one wants to conclude that diesel particulate matter is a toxic air contaminant of special concern for children then one needs to demonstrate that children have an increase in lung cancer. It is possible that children, exposed to low levels of ambient diesel particulate matter, could develop cancer in the time frame indicated by the human epidemiology studies with a latency period of 10-20 years. This would mean that infants exposed to diesel particulate matter should show an increase in lung cancer between the ages of 11-21 (assuming a 1-year-old exposed to diesel particle matter and a latency period of 10-20 years). At the other end of the spectrum, where an older child (12 years) is exposed to diesel particulate matter, there should be noticeable lung cancer in the adult populations of 22-32 (assuming a latency period of 10-20 years). The problem with this analysis is that children are exposed to more than diesel particulate matter. At a minimum the report should evaluate whether there is an increased risk of lung cancer in appropriate age groups that are indicative of possible effects of childhood exposure to diesel particulate matter. The relationship of lung cancer to age shows that the incidence of lung cancer before the age of 35 is barely detectable.[27] Based on the very low incidence of lung cancer in the adult human population between the ages of 15-35 one cannot say that exposure of children to diesel particulate matter causes an increase in lung cancers. Because of the strong relationship of smoking to lung cancer, the time course of cancer rates among smokers and non-smokers should be analyzed separately, if possible.

Response 5: The comment implies that the only reason diesel exhaust is being considered as a TAC that may impact children disproportionately is that it causes lung cancer. This is just one of the reasons described in the report, and probably not the most compelling. As noted in the draft document, diesel exhaust particles have been shown in both humans and animals to exacerbate allergenicity of a number of aeroallergens. In addition, studies of fine particulate matter have shown impacts on the respiratory health of children and there have been associations of PM with low birthweight and infant mortality. Thus, the noncancer impacts alone are sufficient to be concerned about the impacts of diesel exhaust particulate matter on infants and children. Many studies across a range of environments with different sources of PM10 have shown effects of PM10 on

[27] American Lung Association, 2000 www.lungusa.org/data lc/lc_

cardiovascular morbidity and mortality. While these studies focused on the elderly, data from the London smog episode in the early 50's indicate increases in infant mortality associated with the incident.

Comment 6: The draft report indicates in Table 1 that diesel particulate matter is a major source of ambient PAHs and PAHs are of concern because of their potential genotoxic and developmental effects. While it is true that diesel particulate matter contains PAH, the report also lists many others sources of PAH including the following from Table 1 of the appendix section on B(a)P and other PAH; coal-tar pitches, coal-tar, coal gasification, coke production, mineral oils, shale-oils, soots, tobacco smoke, smokeless tobacco products, and aluminum products. As noted above, the EPA estimates all mobile sources were 6 percent of 1996 out-door PAH emissions. There appears to be no reason for singling out diesel particulate matter as a major source of PAH.

Response 6: The fact that there are other sources of PAH is not relevant to listing diesel exhaust particulate as a TAC that may cause infants and children to be especially susceptible to illness.

Comment 7: If the report attributes cancer causation from diesel particulate matter to PAHs because of their potential genotoxic and developmental effects (Table 1), the text should show the mechanisms of action. The report doesn't inform the reader that these chemicals are firmly adsorbed on the particle surface so that they must be extracted from the particle by strong industrial solvents at high temperatures. However, no powerful solvents exist in the lung and the lack of their (PAH) bioavailability in vivo has been documented by experimental data showing that they are not separated from the particles by biological fluids.[28] More recently, a biologically-based ICRP model of lung deposition has also shown that daily deposits of diesel particles in the alveolar-interstitial area of humans exposed for 24 hours to U.S. ambient concentrations of diesel particles

[28] Vostal, J.J., "Bioavailability and Biotransformation of the Mutagenic Component of Particulate Emissions Present in Motor Exhaust Samples", Environmental Health Perspectives, 47: 269-281, 1983;

are extremely low and do not exceed units of picograms (10^{-12} gram/cm^2/day, i.e. levels that are – even in infants and children - completely within the capacity of alveolar clearance mechanisms and easily removed from respiratory airways). Even if the most genotoxic nitro-PAH s adsorbed on Diesel particles (1-10 micrograms per gram) were totally available for desorption in the lung, the resulting concentrations on the alveolar surface would be only at levels of attograms (10^{-18}gram), i.e. levels that cannot exert any genotoxic or non-genotoxic effects.[29]

Not only are such low concentrations of deposited chemical mutagens undetectable in the lung but they cannot be distinguished from lung-deposited PAHs due to other sources. Low ambient air-related lung deposits of diesel particles cannot be, therefore, identified as the only mutagenic risk, even if they are assumed to be completely bioavailable. Moreover, the low levels sharply contrast with the much higher concentrations of particle extracts that produce mutagenic effects in vitro (1-10 µg/ml media) and are used to imply genotoxic action of inhaled PAHs in vivo.

Response 7: The bioavailability of PAHs contained in diesel exhaust was thoroughly reviewed in the diesel exhaust TAC document (ARB, 1998). The studies reviewed clearly indicated that the PAHs in diesel exhaust were bioavailable upon inhalation exposure. Additionally, a recent study by Sato *et al.* (2000) indicated that rats exposed to diesel exhaust by inhalation demonstrated increased mutations in a reporter gene and covalent DNA adducts, additionally suggesting PAH bioavailability. Furthermore, the PAHs in diesel exhaust and other types of exhaust or smoke exist in equilibrium between the particle phase and the vapor phase. Thus, the idea that they are tightly bound to the particles and won't come off in the lung is not supported by what is known of the adsorption-desorption chemistry of PAHs from combustion sources. While total inhaled particle may be low, the linear nature of DNA-adduct and subsequent mutation progressing to cancer is cause for concern for even small doses.

[29] Vostal, J.J., Comments for the Diesel Review Panel of the U.S. EPA Clean Air Scientific Advisory Committee meeting, December 1, 1999;

The fact that there are other sources of PAH in the air does not preclude discussing diesel exhaust particulate in the context of the mandates of SB 25.

Comment 8: Table 1 also indicates that since diesel particulate matter is a contributor to PM_{10} and PM_{10} is thought to exacerbate asthma, then diesel particulate matter should also be considered to exacerbate asthma. There are, however, many constituents of PM_{10} and is not defensible to single out a single component for causing an adverse human health effect without substantiating data. There is limited data suggesting that people exposed to heavy duty truck emissions in urban environments may experience respiratory difficulties but these studies have not directly linked diesel exhaust particles as the causal agent. The Alliance is concerned about these possibilities and supports the Health Effects Institute in their efforts under RFA-00-1 "Effects of Diesel Exhaust and Other Particles on the Exacerbation of Asthma and Other Allergic Diseases" to develop information to either validate or rebut these claims.

Response 8: We are pleased that the Alliance is concerned about the potential of diesel exhaust particulate to exacerbate asthma. A number of studies have shown exacerbation of allergic responses in response to exposure to diesel exhaust particles. In addition, ambient PM is associated with exacerbation of asthma. Since diesel exhaust particles are part and parcel of ambient PM, there is every reason to be concerned about the effects of fine particles whether from a diesel engine or other source.

Comment 9: Finally, as noted in the General Comments, the existing federal and California emissions regulations will reduce diesel PM by 93 % from 1990 to 2020. EPA projects that national annual ambient exposures will be only 0.06 $\mu g/m^3$ by 2020. For all the reasons noted above, it is not clear that there is any substantial risk to adults from current and projected ambient levels of diesel particulate matter. There is also no substantial evidence that infants and children are more at risk than are adults. Therefore, diesel particulate matter should be dropped from consideration as a toxic air contaminant that disproportionately effects children.

Response 9: OEHHA recognizes that diesel exhaust particulate emissions are dropping thanks in large part to efforts of the California Air Resources Board and related industries. We disagree with the comment that there is no substantial risk to either adults or children from ambient exposures. Elevated cancer risks from exposure to ambient levels of diesel exhaust in urban areas (several hundred to 1400 per million) are far above what regulatory agencies consider de minimis (e.g., 1 in one million). Furthermore, as noted in the draft OEHHA document, the presence of PAHs, which are bioavailable, contributes to concern for children. The fine particles that compose diesel exhaust are a recognized component of the ambient PM to which many health effects have now been linked, including impacts on children's lung growth and function. There is, therefore, reason to be concerned that diesel exhaust particulate matter "may cause infants and children to be especially susceptible to illness".

Comments on Specific Substances - Acrolein

Comment 1: Although there is little ambient acrolein data available, there is no reason to believe that motor vehicle-related acrolein has not been reduced along with the other TACs for which data is available.

Response 1: While concentrations of TACs from motor vehicles have declined in California, there is still a problem with smog, from motor vehicles as well as other sources, particularly in the South Coast air basin. Furthermore, modeled concentrations from U.S. EPA (as discussed below by the commenter) suggest that ambient acrolein levels are above the chronic REL, indicating that acrolein is still a health concern. OEHHA's prioritization is based primarily on assessment of the toxicological potential for differential effects, as well as on evidence for significant current exposures in California. Trends in emissions from specific sources will be of interest and germane when the California Air Resources Board examines the need for modified or additional Air Toxics Control Measures.

Comment 2: Acrolein is listed as a proposed Tier 2 TAC on the basis of its irritating properties. The major reasons it was chosen are concern over exacerbation of asthma and the fact that modeled ambient concentrations are above the chronic REL. The evidence for exacerbation of asthma is very weak. OEHHA acknowledges that no direct evidence in humans could be located in the literature. Rather, Borchers et al. made the suggestion that acrolein may exacerbate asthma after finding effects in cell cultures treated with high levels of acrolein. The summary on page 1 of the acrolein appendix indicates "it appears that acrolein may exacerbate asthma." The text of the body of the report leaves out these important qualifiers and indicates on page 7 that "this compound exacerbates asthma and may be a candidate for the top Tier." Such wide extrapolation from a suggestion in the literature is unwarranted.

Response 2*:* Borchers et al. (1999) examined the effect of acrolein on mucus glycoprotein (mucin) gene expression in airway epithelial cells. Cultured human lung cells were treated for 4 hours with 0.01-100 nM acrolein. Borchers et al. reported that *in*

vitro, acrolein can act directly on epithelial cells to increase mucin mRNA levels, or indirectly through inflammatory mediators released after acrolein exposure.

OEHHA disagrees that the evidence for exacerbation of asthma are very weak. It is true that studies have not been conducted that demonstrate a direct link between acrolein exposure and exacerbation of asthma. However, Borchers et al. (1999), primarily a mechanism paper, is not the only study on which we base our conclusion. In vivo studies conducted in several animal species have demonstrated that acrolein can induce airway hyperreactivity, inflammation, and mucus hypersecretion: hallmarks of reactive airway diseases, including asthma.

As discussed in the summary, Lyon et al. (1970) investigated the effects of repeated or continuous exposures of acrolein in rats, guinea pigs, dogs, and squirrel monkeys. Animals were exposed intermittently to 0.7 or 3.7 ppm (1.6 or 8.5 mg/m^3) acrolein for 8 hours/day, 5 days/week for 6 weeks, or continuously to 0.22, 1.0, or 1.8 ppm (0.5, 2.3, or 4.1 mg/m^3) for 90 days. Monkeys and dogs appeared to be the most sensitive to acrolein toxicity. Authors reported finding tracheal squamous metaplasia and basal cell hyperplasia in both monkeys and dogs. Monkeys also exhibited bronchiolitis obliterans with squamous metaplasia in the lungs, while bronchopneumonia was noted in the dogs. Inflammation in the lung interstitiae was more prominent in the dogs than in the monkeys.

Feron et al. (1978) exposed hamsters, rats and rabbits to acrolein vapor at 0, 0.4, 1.4 and 4.9 ppm (0, 0.92, 3.2, and 11.3 mg/m^3) 6 hours/day, 5 days/week for 13 weeks. Acrolein-induced changes in the airways consisted of both destruction and of hyperplasia and metaplasia of the lining epithelium accompanied by inflammatory alterations.

Leikauf et al. (1989) reported acrolein-induced hyperresponsiveness in guinea pigs exposed to 1.3 ppm acrolein for 2 hours. In addition, these authors observed an association between acrolein-induced bronchial hyperresponsiveness and increased sulfidopeptide leukotriene C4 concentration in lung lavage fluid. (Sulfidopeptide

leukotrienes are bronchoconstrictive lipid mediators thought to have an important role in the pathology of asthma.)

Two studies not included in the original summary that add to the overall body of evidence also come from Borchers' laboratory. In Borchers et al. (1998) it was reported that tracheal mucin mRNA and mucin glycoproteins were elevated in lung tissues of rats following *in vivo* exposures to 3 ppm acrolein, 6 hours/day, 5 days/week for 2 weeks *[Borchers MT, Wert SE, Leikauf GD; American J Physiol 1998; 274(4 pt 1):L573-81]*. In mice, exposure to 3 ppm acrolein (6 hours/day, 5 days/week for 3 weeks) resulted in a significant and persistent increase in macrophages, and a rapid but transient increase in neutrophils in bronchoalveolar lavage fluid (indicative of inflammatory response) *[Borchers MT, Wesselkamper S, Wert SE, Shapiro SD, Leikauf GD; Am J Physiol 1999 sept; 277(3pt1):L489-97]*.

In addition to the studies above, it is also important to note that acrolein is an extremely irritating aldehyde, structurally similar to (and more irritating than) formaldehyde which has been associated with the exacerbation of asthma. While studies of acrolein and asthma have not been conducted, acrolein fits the pattern of a chemical that would exacerbate asthma.

OEHHA will change the language on page 7 to match the language on page 1, where it states that acrolein *may* exacerbate asthma.

Comment 3: The summary on page 1 also indicates that acrolein exposures are considerable and that acrolein is a "major contributor to air pollution." The only evidence offered is that modeled concentrations are above the chronic REL. But, as noted above, estimated concentrations greater than health benchmarks should be viewed as an indicator of a potential public health problem and not as characterization of actual health risk. The modeled average ambient concentration of 0.15 $\mu g/m^3$ for 1990 is less than 0.1 ppb. Such a low level cannot be viewed as "considerable" or as a "major contributor to air pollution." Since the lowest observed adverse effect level reported for

eye irritation is 60 ppb, there is no reason to believe that ambient acrolein is a health concern.

Response 3: It is true that exceedance of the REL does not necessarily mean that a health impact will occur. It does imply, however, that the margin of safety built into the REL is being eroded, increasing the possibility that more sensitive individuals in the population may be adversely affected. It is generally impossible to calculate the exact concentration at which anyone in a diverse population would respond to an exposure. Interindividual differences in response and limited information on the toxicant preclude such a determination.

The chronic REL for acrolein is 0.06 $\mu g/m^3$. As noted in the acrolein summary, U.S. EPA modeling data indicate that the estimated statewide annual average ambient concentration of acrolein in California is 0.15 $\mu g/m^3$ (95^{th} percentile = 0.3 $\mu g/m^3$). Pratt et al. (2000) examined U.S. EPA's modeled data, in addition to monitoring data when available, to assess air toxics in Minnesota. Using a hazard quotient approach, the concentrations calculated from the monitoring and modeled data were compared to cancer and noncancer health benchmark values. Pratt et al. (2000) reported that for acrolein (for which there were only modeled data), 70% of the census tracts studied exceeded the health benchmark (in this case, 0.02 $\mu g/m^3$). In addition, Pratt et al. (2000) estimated a screening level total noncancer hazard index by summing all of the noncancer hazard quotients (over all endpoints). They found that acrolein was by far the most important contributor to the noncancer hazard index. The apportionment of the hazard index for an average Minnesotan showed that acrolein accounted for 89% of the hazard index, followed by formaldehyde at 6%, with each of the other pollutants accounting for less than 1% of the hazard index. As part of this study, Pratt et al. also did a comparison of modeling and monitoring data, where possible. While there were no monitoring data available for comparison for acrolein, Pratt et al. did find that overall there was a tendency for the modeling results to underpredict measured values. So, in spite of the uncertainties regarding acrolein concentrations, it does appear that acrolein is a major contributor to respiratory irritation from air pollution, and the modeled concentrations for California, when compared to the REL, indicate a need for attention. The text will be

reworded to indicate that acrolein appears to be a major contributor to respiratory irritation caused by air pollution.

Lastly, concentration alone does not indicate the severity of the risk; toxicity must be considered along with exposure. While acrolein levels may seem low in concentration, the toxicity of the compound indicates that current ambient exposures are a public health concern.

Comment 4: Acrolein is often higher indoors as reported in the draft. To the extent there is any concern over acrolein, that concern should be focused on indoor sources or special situations such as in fires where acrolein concentrations can reach ppm levels and above. The Health Effect Institute has several studies underway to measure human exposures to acrolein and several other aldehydes in different populations and environments. Two studies are also evaluating several biomarkers of aldehyde exposure. When these studies are completed, the information on acrolein as well as other aldehyde levels and exposures will be significantly improved.

Response 4: The modeled concentrations of acrolein (referred to in the comment above) are for outdoor exposures, and are above the chronic REL. OEHHA believes that this is cause for concern. OEHHA agrees that new studies may be able to fill in some of the data gaps regarding exposures to acrolein, and looks forward to seeing any new data as they become available. While indoor air exposures are of general scientific interest to OEHHA, and are important in considering the overall impacts of certain pollutants including acrolein, the primary focus of the SB25 legislation and this prioritization process is outdoor air, whether general ambient levels or hot spots around localized sources. In addition, because the weather is mild in most areas of California, people open their windows. The information obtained from models concerning indoor versus outdoor concentrations for most compounds becomes much less important in scenarios where the windows are open.